REMARKS

With this response, claims 1 and 13 are pending. By way of the present amendment, dependent claim 2 has been cancelled and claim 1 has been amended to incorporate the limitations of dependent claim 2. The specification has also been amended to remove embedded hyperlinks. No new matter enters by way of the present amendments

I. Specification

The disclosure has been objected to as containing embedded hyperlink information. In the Office Action, the Examiner indicates that there is embedded hyperlink information on page 73 of the specification and elsewhere. However, Applicants were unable to locate any such embedded hyperlinks on page 73. As such, clarification may be required. Nonetheless, Applicants have reviewed and amended the specification to remove all embedded hyperlink information evident to Applicants. As such, withdrawal of this objection is respectfully requested.

II. Rejection under 35 U.S.C. § 101, Utility

Claims 2 and 13 stand rejected under 35 U.S.C. § 101 for allegedly not being supported by either specific and/or substantial utility, or a well-established utility. This rejection is respectfully traversed for at least the reasons which follow.

The Examiner alleges that the claimed subject matter is not supported by a credible, specific, and substantial utility because "providing a nucleic acid sequence to a gene that is a putative enzyme does not provide a specific and substantial utility." *Office Action mailed March 13, 2002, Paper No. 17* at page 3. The Examiner further asserts that more research is needed to show that the claimed sequence has enzymatic activity, and that such need for further research indicates that the claimed sequence lacks substantial utility. *See id.* Applicants respectfully disagree.

It is submitted that the Examiner's analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v.*

Orange Bang, Inc., 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

As such, the courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip*, 185 F.3d at 1366, 51 U.S.P.Q.2d at 1702. For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

The present specification describes many objectives that are met by the present invention including, but not limited to providing a substantially purified nucleic acid sequence which encodes a maize enzyme or fragment thereof, wherein the enzyme is a methionine adenosyltransferase (*e.g.*, SEQ ID NO: 1). *See Specification*, Summary of the Invention, page 22. More particularly, the specification provides extensive evidence based on sequence identity (Table A) that the disclosed genes encode polypeptides having specified enzymatic activity. The specification also indicates by way of EC Classification designation that the specified enzyme is of an enzymatic classification well-known in the art. Further, a detailed description of the characterization of the specified enzyme, as well as the identification of such enzyme from other plant sources is provided in the specification. *See, e.g., Specification* at page 10-11. As such, it is submitted that the functionality of the claimed nucleic acid molecules is disclosed. Further, based on the background provided regarding the functionality and structural characteristics of the claimed enzyme, it is submitted that sequence homology is indeed an adequate and predictable indicator of such functionality. Thus, based on such teachings, one of ordinary skill in the art would immediately appreciate the usefulness of the claimed nucleic acid molecules.

The Examiner asserts that the present invention lacks legally sufficient utility because the numerous utilities disclosed are not "substantial". The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v.* Wattanasin, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). "'Practical utility' is a shorthand way of attributing "real world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (CCPA 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use"). *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (CCPA 1974).

Additionally, the Examiner asserts that sound scientific reasoning has been provided based on published art that "sequence homology itself is not enough for having a same function for two sequences." *Office Action mailed March 13, 2002, Paper No. 17* at page 3-4. However, the Examiner provides no evidence specifically relating to the claimed enzyme or the methionine pathway in general. In this regard, an examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). "More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." Federal Register 66(4):1096, Utility Guidelines (2001). "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996).

In sum, Applicants have asserted substantial, specific utilities for the claimed nucleic acid molecules of the invention, and absent specific evidence to the contrary, this assertion must be accepted. The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to encode a protein having methionine adenosyltransferase activity. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from

the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101. Additionally, Applicants have asserted a number of utilities for which the nucleic acids molecules of the invention can be used. These include, but are not limited to, determining the expression levels of the methionine adenosyltransferase (pages 36-39); detecting mutations in the genes encoding these enzymes (page 39-42); and producing plants with altered expression of these enzymes (page 42-47). As such, Applicants have met their burden in establishing specific, "real-world" utilities for the claimed invention.

In view of the above, Applicants submit that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities disclosed in the specification. Accordingly, it is submitted that the rejection of claims 2 and 13 under 35 U.S.C. §101 are improper, and withdrawal of this rejection is respectfully requested.

III. Rejection under 35 U.S.C. § 112, 1st Paragraph, Enablement

Claims 2 and 13 stand rejected under 35 U.S.C. § 112, 1st Paragraph because the claimed invention is allegedly not supported by either a specific and substantial asserted utility or a well established utility, and thus one of ordinary skill in the art would not know how to use the invention. This rejection is traversed for the reasons discussed above with regard to the 35 U.S.C. §101 rejection. As such, it is submitted that the specification enables one of skill in the art to use the invention in accordance with the asserted specific and substantial utilities discussed above. Accordingly, withdrawal of this rejection is respectfully requested.

Moreover, it is submitted that the Examiner has not met the evidentiary burden to impose an enablement rejection for failure to enable one of skill to use the invention. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995) (*quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (CCPA. 1971) (emphasis in original)). It is also well-established that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998)

(emphasis added) (*quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991)).

The present specification indeed discloses how to use the claimed invention as discussed above. The Examiner has failed to provide specific evidence supporting this rejection, or any specific explanation of why the specification allegedly fails to enable these uses. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

Claims 1-2 and 13 also stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. In this regard, the Examiner asserts that undue experimentation would be required to make and use the invention as it is claimed because the specification allegedly fails to "demonstrate the function of a methionine adenosyltransferase . . . and/or analyze the sequence and/or structural conservation of the claimed sequence as compared to those of known methionine adenosyltransferase." *Office Action mailed March 13, 2002, Paper No. 17* at page 7. The Examiner further alleges that "the prior art has demonstrated that assignment of a metabolic gene to a know [sic] function based on homology comparisons provide improper function assignment." *Id.* at page 6. Applicants respectfully traverse these general characterizations.

With regard to the characterization of the prior art as demonstrating unpredictability, the reference relied upon in the Office Action by the Examiner illustrates sequence comparisons with at most 45% sequence homology to known sequences encoding sulfate transporters. However, the presently claimed sequence is shown to have 92% sequence identity to a known methionine adenosyltransferase. *See Specification,* Table A. As such, whatever else the reference does teach, it cannot be said to readily demonstrate the unpredictability of the assignment of methionine adenosyltransferase functionality based on sequence homologies which are significantly higher than those demonstrated in the reference.

Nonetheless, even assuming, *arguendo*, that the Examiner's generalization regarding the unpredictable state of the art is accepted, the conclusion that undue experimentation would be required is inconsistent with the current state of the law. Specifically, the law provides that

experimentation is not necessarily undue simply because it is complex, if the art typically engages in such experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174, (Int'l Trade Comm'n 1983) *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985). Therefore, in the present case, the Examiner's citation to the complex nature of the art only goes to substantiate the fact that experimentation is typical within the art.

A reasonable analysis of the *In re Wands* criteria also supports Applicants position that no undue experimentation would be required to make and use the claimed invention. *See In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998). The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and radiometric synthase assay conditions, to which a person of ordinary skill in the art has access. Performing routine and well-known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (CCPA. 1976).

Moreover, as discussed *supra*, the specification provides evidence based on sequence identity (Table A) that the disclosed genes encode polypeptides having methionine adenosyltransferase activity. Moreover, the specification teaches that the methionine adenosyltransferase enzyme has been characterized from several plant sources, and that nucleic acid molecules have been obtained from a variety of sources. *See Specification* at pages 10-11. Further, the specification discloses that the regulation of methionine adenosyltransferase activity has been observed for an enzyme from soybean, and that the functionality of methionine adenosyltransferase has been experimentally characterized. *See id.* at page 11.. As such, it is submitted that sequence homology is indeed an adequate and predictable indicator of methionine adenosyltransferase functionality, and that one of ordinary skill in the art would clearly understand from the teachings of the specification that the claimed nucleic acid sequences have methionine adenosyltransferase activity without the need for undue experimentation.

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. Again, the specification provides evidence of

sequence identity and discloses general characterizations of methionine adenosyltransferase. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth, fifth, and sixth *Wands* criteria focuses on the nature of the invention, the state of the art, and the relative skill in the art. The present invention relates to nucleic acid and amino acid sequences, and constructs and methods related thereto. Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm, and introduce into other hosts, nucleic acid and amino acid sequences.

The seventh criterion considers the predictability of the art. The Examiner alleges a level of uncertainty involving a functional assignment of metabolic genes based on homology between known and unknown genes. *Office Action mailed March 13, 2002* at page 7. Applicants respectfully disagree and assert, as discussed *supra*, that the specification discloses sufficient guidance to render the results predictable.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). In the present case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, sequence identity data, functional assay, and EC classification, in making that determination.

Accordingly, for at least these reasons, the enablement rejection under 35 U.S.C. § 112, 1st paragraph, is traversed, and withdrawal of this rejection is respectfully requested.

IV. Rejection under 35 U.S.C. § 112, 1st Paragraph, Written Description

Claims 2 and 13 also stand rejected under 35 U.S.C. §112, 1st paragraph, as allegedly containing subject matter which was not described in the specification in a manner that reasonably conveys to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time of filing. This rejection is respectfully traversed for at least the following reasons.

The Office Action acknowledges that SEQ ID NO: 1 meets the written description requirement. However, in support of this rejection, the Office Action alleges:

> there is substantial variability among the species of polynucleotides or nucleic acids encompassed within the scope of the claims because the claimed SEQ ID NO is only a fragment of any full-length gene or cDNA species, or any vector due to the use of the open language 'comprising' or 'consisting essentially'.

Office Action mailed March 13, 2002 at page 5.

Initially, the purpose of the written description requirement is simply to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *See Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, v865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989).

A related and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (CCPA. 1981)). Thus, simply because the claimed nucleic acid sequences may also include sequences from other species does not require that Applicants describe each and every one of these molecules. Further, "a description as filed is presumed to be adequate, unless and until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption." *Federal Register* 66(4):1107, Written Description Guidelines (2001). In this regard, the Examiner is required to disclose "express findings of fact which support the lack of written description conclusion." *Id.*

The present claims are directed to the genus of nucleic acid molecules which encode a specified maize enzyme, or fragments of such enzyme. Applicants have provided detailed chemical structures of the claimed nucleic acid sequences, as well as additional information about the encoded enzymes. These sequences provide "structural feature[s] possessed by members of the [claimed] genus that distinguish them from others." *Regents of the University of*

California v. Eli Lilly and Co., 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). In contrast to the mere name "cDNA" provided in *Eli Lilly*, Applicants have provided detailed chemical structures. For at least this reason, it is respectfully submitted that the present claims meet the written description provision under 35 U.S.C. § 112, 1st paragraph.

The use of open claiming language (comprising) or semi-open claiming (consisting essentially of) does not alter the fact that a skilled artisan would readily envision adequate written description support. Contrary to the allegations raised in the Office Action regarding the "substantial variability" among the claimed species, it is submitted that the claimed species are adequately defined by the recitation of the specific sequence of SEQ ID NO: 1. As such, the claims to not encompass "any full-length gene or cDNA species, or any vector," rather the claims encompass only those molecules which include the structural sequence of SEQ ID NO: 1. The fact that nucleic acid sequences may be added to either end of the recited sequence is beside the point. Applicants have therefore reasonably conveyed to one skilled in the art possession of the claimed invention, even when additional sequences are added to either end. Indeed, as disclosed in the specification on pages 53, the addition of, *e.g.*, detectable labels or extra nucleotides is readily envisioned by those of ordinary skill upon reading the present specification.

Additionally, "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'" *Eli Lilly*, 119 F.3d at 1569. In the present case, it is submitted that the disclosure of an extensive number of nucleic acid sequences encoding the specified enzyme or fragments thereof, *e.g.*, SEQ ID NOS: 1-429 and 1635-2479, in combination with "other appropriate language" in fact does provide sufficient written description for claims within the genus. Such "other appropriate language" is found, *e.g.*, in the form of sequence identity and numerous methodologies to obtain additional sequences. Therefore, it is clear that one of ordinary skill in the art would recognize that Applicants were in possession of the genus of the specified maize enzyme encoding genes.

Accordingly, for at least the foregoing reasons, the rejection under 35 U.S.C.. §112, 1st paragraph, written description, is traversed, and withdrawal of this rejection is respectfully requested.

V. Rejection under 35 U.S.C. § 102

Claim 1 stands rejected under 35 U.S.C. §102 as allegedly anticipated by Everett *et al.* The rejection is respectfully traversed.

"It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Further, "an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device." *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q. 619 (Fed. Cir. 1985).

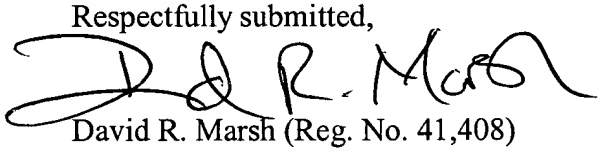
Claim 1 has been amended to incorporate the limitations of dependent claim 2. As such, claim 1 as amended recites the sequence of SEQ ID NO: 1. Whatever else Everett does teach, it fails to teach the recited nucleic acid sequence in its entirety. Absent a teaching of each and every element of the claim, *i.e.*, SEQ ID NO: 1, the reference cited by the Examiner does not anticipate claim 1. Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance, and notice of such is respectfully requested.

The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,



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Marked up version of the specification and claims

In the specification:

Homologues in other organisms are available that can be used for comparative sequence analysis. Multiple alignments are performed to study similarities and differences in a group of related sequences. CLUSTAL W is a multiple sequence alignment package that performs progressive multiples sequence alignments based on the method of Feng and Doolittle, *J. Mol. Evol.* 25:351-360 (1987), the entirety of which is herein incorporated by reference. Each pair of sequences is aligned and the distance between each pair is calculated; from this distance matrix, a guide tree is calculated and all of the sequences are progressively aligned based on this tree. A feature of the program is its sensitivity to the effect of gaps on the alignment; gap penalties are varied to encourage the insertion of gaps in probable loop regions instead of in the middle of structured regions. Users can specify gap penalties, choose between a number of scoring matrices, or supply their own scoring matrix for both pairwise alignments and multiple alignments. CLUSTAL W for UNIX and VMS systems is available at: [ftp.ebi.ac.uk] ftp.ebi.ac.uk. Another program is MACAW (Schuler *et al.*, *Proteins Struct. Func. Genet.* 9:180-190 (1991), the entirety of which is herein incorporated by reference, for which both Macintosh and Microsoft Windows versions are available. MACAW uses a graphical interface, provides a choice of several alignment algorithms and is available by anonymous ftp at: [ncbi.nlm.nih.gov] ncbi.nlm.nih.gov (directory/pub/macaw).

A PCR probe is a nucleic acid molecule capable of initiating a polymerase activity while in a double-stranded structure [to] with another nucleic acid. Various methods for determining the structure of PCR probes and PCR techniques exist in the art. Computer generated searches using programs such as Primer3 ([www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi] www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi), STSPipeline ([www-genome.wi.mit.edu/cgi-bin/www-STS_Pipeline] www-genome.wi.mit.edu/cgi-bin/www-STS_Pipeline) or GeneUp (Pesole *et al.*, *Biotechniques* 25:112-123 (1998) the entirety of which is herein incorporated by reference), for example can be used to identify potential PCR primers.

In the claims:

1. (Twice Amended) A substantially purified nucleic acid molecule that encodes a maize [or a soybean] enzyme or fragment of said maize [or soybean] enzyme, wherein said maize [or soybean] enzyme is Methionine Adenosyltransferase and wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO: 1.